



Chromosomal abnormalities in isolated persistent left superior vena cava: A systematic review and meta-analysis

İzole persistan sol superior vena kavada kromozom anomalileri: Sistematik bir derleme ve meta-analiz

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Abstract

Persistent left superior vena cava (PLSVC) is the most common systemic venous anomaly detected prenatally, yet the risk of chromosomal abnormalities in truly isolated cases remains uncertain. This systematic review and meta-analysis aimed to determine the rate of chromosomal anomalies in fetuses with isolated PLSVC by including only fetuses who underwent chromosomal analysis. A systematic search of PubMed/MEDLINE, EMBASE, and the Cochrane Library was performed from January 2000 through March 2026. Studies reporting chromosomal data for fetuses with sonographically confirmed isolated PLSVC were eligible. Isolated PLSVC was defined as PLSVC in the absence of intracardiac or extracardiac structural anomalies, irrespective of the presence of the right superior vena cava. Only isolated fetuses with prenatal or postnatal chromosomal analysis were included; untested fetuses were not assumed to be chromosomally normal. The pooled proportion was calculated as the total number of events divided by the total number of genetically assessed isolated fetuses, with 95% confidence intervals (CIs) calculated using the Wilson score method. Twelve studies were included, comprising 892 isolated PLSVC fetuses, of whom 302 underwent genetic testing. Eight chromosomal anomalies were identified, yielding a pooled chromosomal anomaly rate of 2.6% (95% CI: 1.3-5.1%). In the leave-one-out sensitivity analysis, the pooled rate ranged from 1.3% to 4.8%. The risk of chromosomal abnormalities in isolated PLSVC is low but not negligible. Because genetic testing was performed more often in higher-risk pregnancies, this estimate probably overestimates the background risk. The available evidence does not support a universal recommendation for invasive prenatal diagnosis based solely on an isolated PLSVC; decision-making should be individualized based on maternal age, serum screening or cell-free DNA results, nuchal translucency, detailed fetal anatomical assessment, and patient preference.

Keywords: Persistent left superior vena cava, chromosomal anomaly, prenatal diagnosis, meta-analysis, systematic review

Öz

Persistan sol superior vena kava (PLSVC), prenatal dönemde en sık saptanan sistemik venöz anomali; ancak gerçek izole olgularda kromozom anomalisi riski belirsizliğini korumaktadır. Bu sistematik derleme ve meta-analizin amacı, yalnızca kromozom analizi yapılan fetüsleri dahil ederek izole PLSVC'de kromozom anomalisi oranını belirlemektir. PubMed/MEDLINE, EMBASE ve Cochrane Kütüphanesi Ocak 2000-Mart 2026 tarihleri arasında tarandı. Ultrasonografik olarak doğrulanmış izole PLSVC olgularında kromozom verisi bildiren çalışmalar dahil edildi. İzole PLSVC, sağ superior vena kava varlığından bağımsız olarak, intrakardiyak veya ekstrakardiyak yapısal anomali eşlik etmeyen PLSVC olarak tanımlandı. Yalnızca prenatal veya postnatal kromozom analizi yapılan izole fetüsler değerlendirildi; test edilmeyen fetüsler kromozomal olarak normal kabul edilmedi. Havuzlanmış oran, toplam olay sayısının genetik olarak değerlendirilen toplam izole fetus sayısına bölünmesiyle hesaplandı; %95 güven aralıkları (GA) Wilson skor yöntemiyle belirlendi. On iki çalışma dahil edildi; bu çalışmalarda 892 izole PLSVC fetüsü bulunuyordu ve bunların 302'sine genetik inceleme yapılmıştı. Toplam 8 kromozom anomalisi saptandı ve havuzlanmış kromozom anomalisi oranı %2,6 (%95 GA: %1,3-5,1) olarak bulundu. Bırak-bir-çıkartma duyarlılık analizinde havuzlanmış oran %1,3 ile %4,8 arasında değişti. İzole PLSVC'de kromozom anomalisi riski düşük ancak ihmal edilemez düzeydedir. Genetik inceleme daha çok yüksek riskli gebeliklerde yapıldığından bu oran, gerçek arka plan riskini büyük olasılıkla olduğundan yüksek göstermektedir. Mevcut kanıtlar, yalnızca izole PLSVC varlığına dayanarak genel bir invaziv prenatal tanı önerisini desteklememektedir; karar maternal yaş, tarama testleri veya hücresiz DNA sonuçları, ense saydamlığı, ayrıntılı fetal anatomik değerlendirme ve hasta tercihi dikkate alınarak bireyselleştirilmelidir.

Anahtar Kelimeler: Persistan sol superior vena kava, kromozom anomalisi, prenatal tanı, meta-analiz, sistematik derleme

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Received/Geliş Tarihi: 25.05.2026 Accepted/Kabul Tarihi: 12.10.2026 Epub: 20.10.2026

Cite this article as: Sarıdaş Demir S, Demir B. Chromosomal abnormalities in isolated persistent left superior vena cava: a systematic review and meta-analysis. Turk J Obstet Gynecol. [Epub Ahead of Print]



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Introduction

Persistent left superior vena cava (PLSVC) is the most common thoracic systemic venous anomaly and usually results from the persistence of the left anterior cardinal vein. In most fetal cases, bilateral superior vena cava are present and the left superior vena cava drains into the right atrium through a dilated coronary sinus⁽¹⁾. PLSVC is estimated to occur in approximately 0.2-0.5% of low-risk fetal populations and in up to 9% of fetuses with congenital heart disease⁽²⁾, underscoring its frequent association with structural cardiac anomalies and the clinical importance of distinguishing isolated from non-isolated cases.

Prenatal detection of PLSVC has increased with the routine use of the three-vessel and tracheal view. The finding appears as an additional vessel located to the left of the pulmonary artery. Once PLSVC is identified, the most important clinical step is to distinguish truly isolated PLSVC from PLSVC associated with intracardiac anomalies, extracardiac anomalies, heterotaxy, or aortic arch abnormalities⁽³⁾.

The need for invasive prenatal genetic testing in cases of isolated PLSVC remains controversial. The influential 2016 meta-analysis by Gustapane et al.⁽⁴⁾ reported an approximately 7% rate of chromosomal anomalies in isolated PLSVC, but this estimate was largely based on small high-risk referral cohorts. Since then, larger cohorts from low-risk or mixed screening settings have become available. In addition, some studies reported all isolated cases, although chromosomal analysis was performed only on a subgroup; treating untested cases as chromosomally normal would underestimate the risk.

Therefore, the aim of this systematic review and meta-analysis was to estimate the chromosomal anomaly rate in isolated PLSVC, including only fetuses who underwent chromosomal analysis and to provide a cautious clinical interpretation to inform prenatal counseling.

Materials and Methods

Ethical Considerations

This study is a systematic review and meta-analysis of published aggregate data; no primary patient data were collected. Ethics committee approval was not required. The study was conducted in accordance with the ethical standards described in the Declaration of Helsinki (revised 2024). Individual patient informed consent was not applicable.

Protocol and Registration

This systematic review and meta-analysis was conducted according to PRISMA 2020⁽⁵⁾ and MOOSE⁽⁶⁾ recommendations. The protocol was registered in PROSPERO (CRD420261416967). The protocol was prospectively registered under the broader title “Genetic and Perinatal Outcomes of Isolated Persistent Left Superior Vena Cava.” The current analysis focuses on chromosomal anomaly rates in the genetically assessed isolated subgroup; analyses of perinatal outcomes and copy-number variants are planned as separate reports. The requirement for

bilateral superior vena cavae was removed from the definition of isolated PLSVC, deviating from the registered protocol.

Eligibility Criteria

Studies were eligible if they reported fetuses with sonographically confirmed PLSVC and provided extractable chromosomal data for isolated cases. In this study, isolated PLSVC was defined in a clinical/structural sense rather than an anatomical one, as a PLSVC without associated intracardiac or extracardiac structural anomalies, regardless of the presence or absence of the right superior vena cava. Case reports, narrative reviews, conference abstracts, and duplicate cohorts were excluded.

Exclusion Criteria

Studies were excluded if they lacked prenatal PLSVC data; were postnatal-only or adult-only; were case reports, reviews, editorials, letters, or conference abstracts; were technical imaging studies without eligible outcome data; or did not provide extractable data for isolated PLSVC. Studies were also excluded when the isolated PLSVC subgroup could not be separated from non-isolated cases or when chromosomal outcomes were not reported for isolated cases. In the case of overlapping cohorts, the most recent, largest, or most complete report was retained.

Search Strategy

A systematic search was performed from January 2000 to March 2026 in PubMed/MEDLINE, EMBASE, and the Cochrane Library using the following search strategy: (“persistent left superior vena cava” OR “PLSVC” OR “bilateral superior vena cava”) AND (“chromosome*” OR “karyotype*” OR “aneuploid” OR “prenatal”). Reference lists of relevant reviews and included articles were hand-searched.

Data Extraction

Two reviewers independently extracted study characteristics, study setting, total PLSVC cases, isolated PLSVC cases, genetically tested isolated PLSVC cases, chromosomal anomalies, and genetic investigation methods. The primary analysis included only fetuses with isolated PLSVC who underwent genetic testing. Genetic testing, performed either prenatally or postnatally, was accepted. Clinically isolated fetuses without genetic testing were not considered chromosomally normal.

Chromosomal events occurring only in non-isolated groups were not attributed to the isolated cohort. Copy-number variants detected by chromosomal microarray were counted as chromosomal abnormalities only if classified as pathogenic or likely pathogenic by the original study authors. This definition was applied consistently across all included studies, and variants of uncertain significance were not counted as events.

Statistical Analysis

The primary outcome was the proportion of genetically assessed fetuses with isolated PLSVC who had a chromosomal anomaly. Because events were rare and most studies contributed small denominators, the pooled proportion was calculated as the total

number of events divided by the total number of genetically assessed isolated fetuses. The 95% confidence intervals (CIs) for the pooled and individual study proportions were calculated using the Wilson score method. Between-study heterogeneity was assessed using Cochran's Q and I^2 statistics calculated on Freeman-Tukey double arcsine transformed proportions⁽⁷⁾. The crude pooled proportion does not incorporate between-study heterogeneity, which is acknowledged as a limitation. An exploratory funnel plot is provided in Supplementary Figure S1; formal tests of funnel-plot asymmetry were not performed because the number of studies and events was insufficient for a meaningful evaluation. Analyses were performed in Python. A leave-one-out sensitivity analysis was performed to evaluate the influence of individual studies on the primary pooled estimate. Each study was sequentially excluded, and the pooled proportion was recalculated for the remaining $k-1$ studies.

Risk of Bias and Quality Assessment

The methodological quality and risk of bias of the included observational studies were assessed independently by two reviewers using an 8-domain framework adapted from the Joanna Briggs Institute critical appraisal tools for prevalence studies and case series. The domains were: sampling frame; inclusion criteria; validity of PLSVC diagnosis; definition of isolation; completeness of follow-up; ascertainment of chromosomal outcome; statistical analysis; and participation rate. Overall risk of bias was categorized as low (6-8 "yes" responses), moderate (4-5), or high (≤ 3). Disagreements were resolved through discussion and consensus. Studies were not excluded solely on the basis of quality assessment. As the official Joanna Briggs Institute tools do not specify this scoring format, the authors adapted it (Supplementary Table S1).

Results

Study Selection

The initial search yielded 1,103 records. After the removal of 394 duplicates, 709 records were screened by title and abstract, and 666 were excluded. Forty three full-text reports were assessed for eligibility; 31 were excluded. Twelve studies were included in the quantitative synthesis, comprising 2,314 PLSVC cases, of which 892 were classified as isolated. Genetic testing was performed on 302 isolated fetuses, and 8 chromosomal abnormalities were identified. Chaoui et al.⁽⁸⁾ and Head et al.⁽⁹⁾ were excluded because they did not provide extractable chromosomal outcome data for an isolated PLSVC subgroup. Durand et al.⁽¹⁰⁾ reported aortic coarctation outcomes without extractable isolated PLSVC chromosomal data. Esin et al.⁽¹¹⁾ was excluded because karyotyping was recommended but not performed in isolated cases; chromosomal status in these fetuses was considered normal on the basis of neonatal examination findings rather than genetic testing. Du et al.⁽¹²⁾ was excluded because, in fetuses without prenatal karyotyping, the karyotype was assumed to be normal if the newborn appeared clinically

normal; consequently, the 44 isolated PLSVC fetuses (two with an abnormal karyotype) could not be separated into genetically tested and clinically presumed normal cases, and the number of genetically tested isolated fetuses could not be determined. Berg et al.⁽³⁾ was excluded because karyotype results were reported only for syndromic cases; genetic testing of the seven isolated PLSVC fetuses was not reported, and the number of genetically tested isolated fetuses could not be determined. The PRISMA flow diagram is presented in Figure 1.

Study Characteristics

The 12 included studies were published between 2002 and 2026 and comprised a total of 2,314 fetuses with PLSVC, of whom 892 were classified as having isolated PLSVC. Four studies were conducted in China, three in Türkiye, two in France, and one each in Belgium, Korea, and Canada. Of the 12 studies, 11 were retrospective and one [Durand et al.⁽¹³⁾] was prospective. Genetic testing was performed in 302 of the 892 isolated fetuses (33.9%), and the proportion of isolated fetuses tested ranged from 1.8% to 100% across studies. Conventional karyotyping was the only genetic method in seven studies, whereas chromosomal microarray or copy-number variation sequencing was used either alone or together with karyotyping in five studies. The characteristics of the included studies are presented in Table 1.

Risk of Bias and Quality Assessment

Of the 12 included studies, 6 were rated as low risk of bias [Barrea et al.⁽¹⁴⁾, Esmer et al.⁽¹⁵⁾, Özsürmeli et al.⁽¹⁶⁾, Durand et al.⁽¹³⁾, Cao et al.⁽¹⁷⁾, Kahramanoğlu et al.⁽¹⁸⁾], 5 as moderate risk [Machevin-Surugue et al.⁽¹⁹⁾, Choi et al.⁽²⁰⁾, Minsart et al.⁽²¹⁾, Li and Wu⁽²²⁾, Wei et al.⁽²³⁾], and 1 as high risk [Yang et al.⁽²⁴⁾]. The principal sources of methodological concern were incomplete genetic testing of isolated fetuses and variable definitions of isolation. No study was excluded on the basis of quality rating alone (Supplementary Table S1).

Meta-analysis Results

Overall, eight chromosomal abnormalities were identified among 302 genetically tested, isolated PLSVC fetuses, corresponding to a crude chromosomal abnormality rate of 2.6% (95% CI: 1.3-5.1%). Between-study heterogeneity was moderate (Cochran's $Q=17.5$, $df=11$, $p=0.094$; $I^2=37\%$). Eight of the 12 studies contributed no events to the analysis. Among the eight chromosomal abnormalities reported in fetuses with isolated PLSVC, two were trisomy 21 and one was a pathogenic 1q21.1q21.2 microduplication. The remaining five abnormalities were reported by Wei et al.⁽²³⁾; however, the specific chromosomal diagnoses of these five isolated cases were not individually provided. Therefore, the exact chromosomal spectrum of these five cases could not be determined from the available data. The forest plot is shown in Figure 2.

Sensitivity Analysis

In the leave-one-out analysis, the pooled rate ranged from 1.3% (95% CI: 0.4-3.6%) when Wei et al.⁽²³⁾ was excluded to 4.8%

(95% CI: 2.4-9.1%) when Li and Wu⁽²²⁾ was excluded. Exclusion of any other single study yielded pooled rates between 2.4% and 2.8%. Wei et al.⁽²³⁾ contributed five of the eight events, whereas Li and Wu⁽²²⁾ reported no chromosomal abnormalities in the isolated PLSVC group.

Publication Bias and Small-study Assessment

An exploratory funnel plot is shown in Supplementary Figure S1.

Discussion

This systematic review and meta-analysis estimates the rate of chromosomal anomalies in genetically assessed fetuses with isolated PLSVC to be 2.6% (95% CI: 1.3-5.1%). This rate is lower than the 7.0% estimate reported in the 2016 meta-analysis⁽⁴⁾, and the upper limit of its CI remains below that figure. This difference likely reflects the inclusion of more recent and larger cohorts, including low-risk and mixed screening populations. Consistent with this low estimate, a cohort in which all isolated PLSVC fetuses were karyotyped reported no chromosomal anomalies (0/14)⁽²⁵⁾; although this study was not included in the pooled analysis because it was available only as a conference

abstract, its findings support the low risk observed in the present analysis.

Of the 892 clinically isolated fetuses in the included studies, only 302 (33.9%) underwent chromosomal analysis.

The clinical implications are balanced. Isolated PLSVC should not be treated in the same way as non-isolated PLSVC, which is associated with a higher risk of genetic and structural abnormalities. However, the risk in isolated cases is not zero. The most defensible counseling approach involves individualized decision-making that takes into account maternal age, first-trimester screening, cell-free DNA, nuchal translucency measurement, detailed anatomic survey, cardiac assessment, and parental preference. In practice, a normal first-trimester combined screening result or a low-risk cell-free DNA result substantially reduces the residual risk of common aneuploidies and may reasonably support a non-invasive approach, although it does not exclude submicroscopic copy-number variants. By contrast, an abnormal screening result, an increased nuchal translucency, or any subtle additional finding on detailed fetal echocardiography should prompt reconsideration of invasive testing. When invasive testing is pursued, chromosomal microarray rather than conventional karyotyping is the preferred

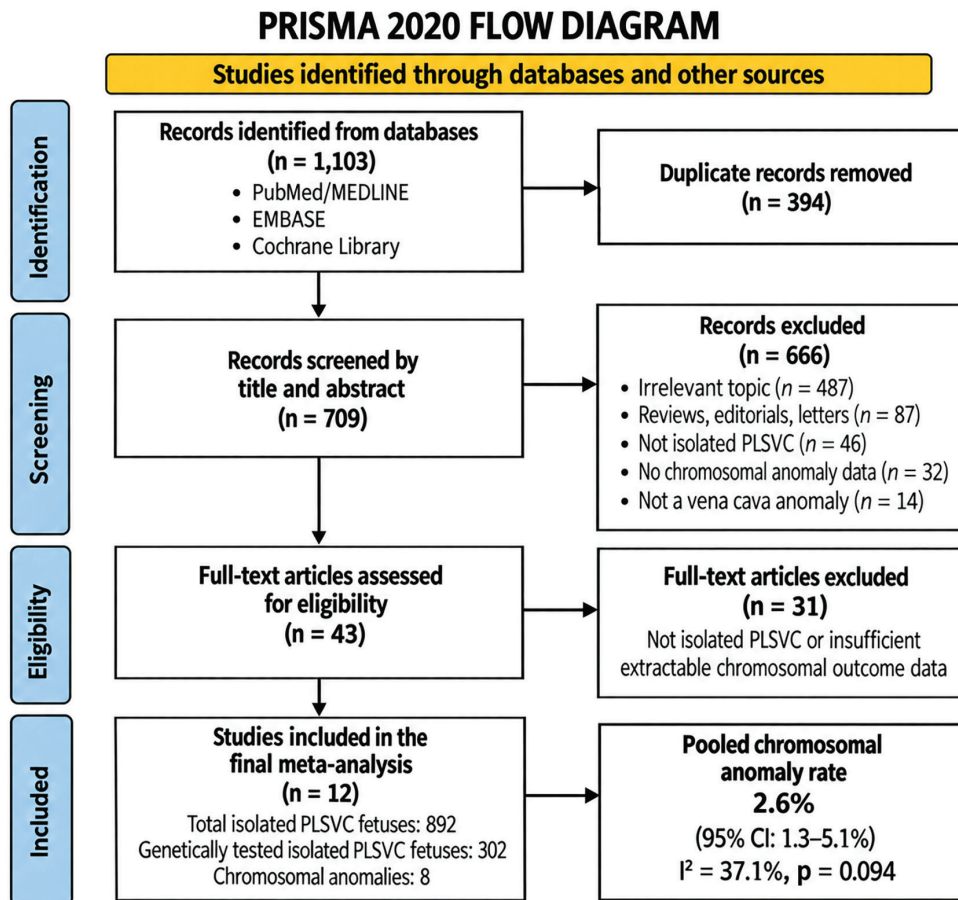


Figure 1. PRISMA 2020 flow diagram illustrating the corrected study selection process

CI: Confidence interval, PLSVC: Persistent left superior vena cava

platform because most included studies relied on karyotyping, and submicroscopic abnormalities may otherwise be missed. No single threshold applies uniformly: the counseling discussion should explicitly convey the low but non-negligible background risk identified here, contextualize it alongside the patient's other screening results, and incorporate parental risk tolerance before a shared decision is reached.

The available data suggest that the genetic spectrum associated with isolated PLSVC may include both common aneuploidies and submicroscopic copy-number variants. In the present analysis, trisomy 21 was reported in two cases, while Cao et al.⁽¹⁷⁾ identified a pathogenic 1q21.1q21.2 microduplication. Although Wei et al.⁽²³⁾ did not provide the individual chromosomal diagnoses of the five abnormal cases in their isolated PLSVC

Table 1. Characteristics and chromosomal anomaly data of included studies

Study	Country	Design	Total PLSVC	Isolated PLSVC	Genetically tested isolated	Events	Genetic test
Machevin-Surugue et al. ⁽¹⁹⁾ (2002)	France	Retro	22	8	5	0	Karyotype
Barrea et al. ⁽¹⁴⁾ (2011)	Belgium	Retro	19	10	6	1	Karyotype
Esmer et al. ⁽¹⁵⁾ (2014)	Türkiye	Retro	31	8	6	0	Karyotype
Choi et al. ⁽²⁰⁾ (2016)	Korea	Retro	65	34	8	1	Karyotype
Özsürmeli et al. ⁽¹⁶⁾ (2019)	Türkiye	Retro	32	8	2	0	Karyotype
Minsart et al. ⁽²¹⁾ (2020)	Canada	Retro	229	39	6	0	aCGH/karyotype
Cao et al. ⁽¹⁷⁾ (2022)	China	Retro	140	51	51	1	CMA
Durand et al. ⁽¹³⁾ (2022)	France	Prosp	256	113	2	0	Karyotype
Yang et al. ⁽²⁴⁾ (2023)	China	Retro	97	49	5	0	Karyotype/CNV-seq
Kahramanoğlu et al. ⁽¹⁸⁾ (2024)	Türkiye	Retro	100	14	13	0	Karyotype/array
Li and Wu ⁽²²⁾ (2025)	China	Retro	425	307	134	0	Karyotype
Wei et al. ⁽²³⁾ (2026)	China	Retro	898	251	64	5	aCGH/karyotype
Total			2314	892	302	8	

aCGH: Array comparative genomic hybridization, CMA: Chromosomal microarray analysis, CNV-seq: Copy-number variation sequencing, PLSVC: Persistent left superior vena cava, Prosp: Prospective, Retro: Retrospective

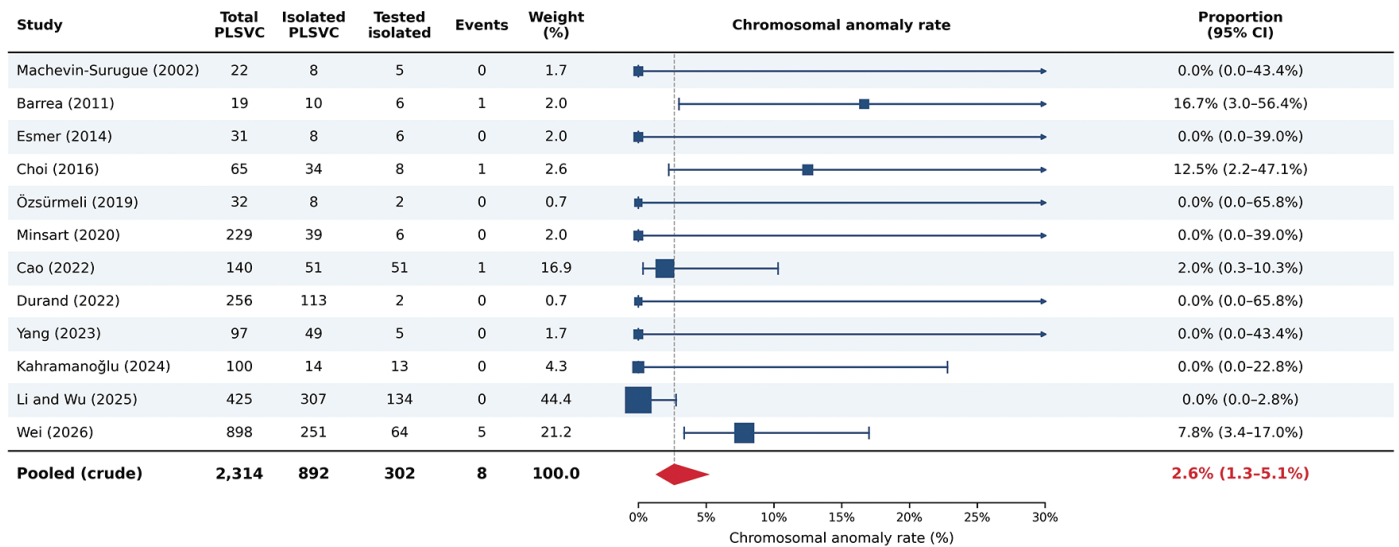


Figure 2. Forest plot of chromosomal anomaly proportions in genetically assessed isolated PLSVC fetuses. The pooled estimate is the crude proportion (8/302); individual-study and pooled 95% CIs were calculated using the Wilson score method

CI: Confidence interval, PLSVC: Persistent left superior vena cava

subgroup, the authors noted that chromosomal abnormalities associated with isolated PLSVC may predominantly involve microdeletions or microduplications. This observation highlights the potential relevance of submicroscopic copy-number variants and underscores the importance of detailed case-level genetic reporting in future studies evaluating isolated PLSVC.

Beyond the comparison with Gustapane et al.⁽⁴⁾, the individual cohorts included here show variability that merits discussion. Eight of the 12 studies contributed no events, whereas a single cohort [Wei et al.⁽²³⁾] contributed five of the eight anomalies observed. In the leave-one-out analysis, the pooled rate ranged from 1.3% after exclusion of Wei et al.⁽²³⁾ to 4.8% after exclusion of Li and Wu⁽²²⁾. Li and Wu⁽²²⁾ reported no chromosomal abnormalities in the isolated PLSVC group. The pooled estimate should therefore be interpreted as a range of plausible risks, rather than a precise value. This pattern may reflect differences in referral or workup practices, rather than a true difference in underlying risk. Differences in genetic testing strategy (karyotype alone versus karyotype plus microarray), population source (referral versus routine screening), and regional screening infrastructure likely contribute to the variability across studies and should be considered when extrapolating the pooled estimate to a specific clinical setting.

The strengths of this analysis include a registered protocol, PRISMA-based reporting, a predefined definition of isolation, and inclusion of only genetically tested fetuses. Limitations include the retrospective design of most included studies, variable genetic testing strategies, possible selection bias regarding who underwent invasive testing, a small absolute number of events, and the use of aggregate rather than individual-patient data. The crude pooled proportion does not account for between-study heterogeneity. In some studies, it could not be determined whether isolated fetuses reported as chromosomally normal had actually been tested, or had been assumed to be normal on the basis of a clinically normal newborn. Three cohorts were excluded because normality in isolated fetuses was partly based on clinical assessment or genetic testing of isolated fetuses was not reported, so that the number of genetically tested isolated fetuses could not be determined [Esin et al.⁽¹¹⁾, Du et al.⁽¹²⁾, and Berg et al.⁽³⁾]. Notably, Du et al.⁽¹²⁾ reported two chromosomal anomalies among isolated fetuses; its exclusion may have slightly lowered the pooled estimate. Furthermore, most included studies predate the routine use of chromosomal microarray or copy-number variant sequencing; therefore, the pooled estimate is largely based on conventional karyotyping and may underestimate the true rate of submicroscopic chromosomal abnormalities.

A critical limitation warrants a dedicated discussion. The analysis was based primarily on genetically tested isolated PLSVC fetuses, rather than on all such fetuses identified sonographically. Because invasive testing was typically driven by concurrent risk factors (advanced maternal age, abnormal serum

screening, abnormal nuchal translucency, or parental request), the genetically assessed subgroup was systematically enriched for higher-risk pregnancies. This indication bias (workup bias) means that the pooled estimate of 2.6% likely overestimates the true background rate of chromosomal anomalies in unselected, low-risk, isolated PLSVC pregnancies. Prospective cohort studies that offer standardized genetic evaluation to all isolated PLSVC cases, regardless of concurrent risk factors, are required to establish the true population-level rate.

Conclusion

In genetically tested fetuses with sonographically isolated PLSVC, the pooled chromosomal anomaly rate is approximately 2.6% (95% CI: 1.3-5.1%). Because genetic testing was more often performed in higher-risk pregnancies, this rate likely overestimates the background risk in unselected pregnancies. The available evidence does not support a universal recommendation for invasive prenatal diagnosis based solely on isolated PLSVC. A comprehensive risk assessment incorporating maternal age, serum screening or cell-free DNA, nuchal translucency, detailed anatomic evaluation, and patient preference should guide counseling; individualized decision-making remains the most appropriate management strategy. If invasive testing is selected, chromosomal microarray analysis may be considered in accordance with current prenatal genetic practice.

Ethics

Ethics Committee Approval: This study is a systematic review and meta-analysis of published aggregate data. No primary patient data were collected; therefore, ethics committee approval was not required. The study was conducted in accordance with the Declaration of Helsinki (revised 2024).

Informed Consent: Not required.

Acknowledgments

The authors sincerely thank Abdülmecit Karakaş for his valuable support in reviewing the statistical analyses and his helpful comments during the revision process.

Footnotes

Authorship Contributions

Concept: S.S.D., B.D., Design: S.S.D., B.D., Data Collection or Processing: S.S.D., B.D., Analysis or Interpretation: S.S.D., B.D., Literature Search: S.S.D., B.D., Writing: S.S.D., B.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: AI tools were used just for text editing, language correction, data analysis, and literature assistance. The authors reviewed and verified all AI-assisted content and take

full responsibility for the accuracy, integrity, and final content of the manuscript.

Supplementary Figure Link: <https://d2v96fxpocvxx.cloudfront.net/f942abf9-a73b-4057-b48b-c3a4b7d0c2a5/content-images/b8893180-cb40-414b-a859-4643cb7c15bf.pdf>

Supplementary Table Link: <https://d2v96fxpocvxx.cloudfront.net/f942abf9-a73b-4057-b48b-c3a4b7d0c2a5/content-images/60e87604-1acc-4d50-b0f2-ac123e27a205.pdf>

References

1. Tyrak KW, Holda J, Holda MK, Koziej M, Piatek K, Klimek-Piotrowska W. Persistent left superior vena cava. *Cardiovasc J Afr*. 2017;28:e1-4.
2. Lopes KRM, Bartsota M, Doughty V, Carvalho JS. Single left superior vena cava: antenatal diagnosis, associated anomalies and outcomes. *Ultrasound Obstet Gynecol*. 2022;60:640-5.
3. Berg C, Knüppel M, Geipel A, Kohl T, Krapp M, Knöpfle G, et al. Prenatal diagnosis of persistent left superior vena cava and its associated congenital anomalies. *Ultrasound Obstet Gynecol*. 2006;27:274-80.
4. Gustapane S, Leombroni M, Khalil A, Giacci F, Marrone L, Bascietto F, et al. Systematic review and meta-analysis of persistent left superior vena cava on prenatal ultrasound: associated anomalies, diagnostic accuracy and postnatal outcome. *Ultrasound Obstet Gynecol*. 2016;48:701-8.
5. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
6. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000;283:2008-12.
7. Freeman MF, Tukey JW. Transformations related to the angular and the square root. *Ann Math Stat*. 1950;21:607-11.
8. Chaoui R, Heling KS, Kalache KD. Caliber of the coronary sinus in fetuses with cardiac defects with and without left persistent superior vena cava and in growth-restricted fetuses with heart-sparing effect. *Prenat Diagn*. 2003;23:552-7.
9. Head CE, Jowett VC, Sharland GK, Simpson JM. Timing of presentation and postnatal outcome of infants suspected of having coarctation of the aorta during fetal life. *Heart*. 2005;91:1070-4.
10. Durand I, Deverriere G, Thill C, Lety AS, Parrod C, David N, et al. Prenatal detection of coarctation of the aorta in a non-selected population: a prospective analysis of 10 years of experience. *Pediatr Cardiol*. 2015;36:1248-54.
11. Esin D, Aslan Çetin B, Şenol G, Selçuki NFT, Gedik Özköse Z, Acar Z, et al. Clinical significance of prenatally diagnosed persistent left superior vena cava. *J Gynecol Obstet Hum Reprod*. 2022;51:102332.
12. Du L, Xie HN, Zhu YX, Li LJ, Peng R, Zheng J. Fetal persistent left superior vena cava in cases with and without chromosomal anomalies. *Prenat Diagn*. 2014;34:797-802.
13. Durand I, Hazelzet T, Gillibert A, Parrod C, David N, El Youssef F, et al. Outcomes following prenatal diagnosis of isolated persistent left superior vena cava. *Arch Cardiovasc Dis*. 2022;115:335-47.
14. Barrea C, Ovaert C, Moniotte S, Biard JM, Steenhaut P, Bernard P. Prenatal diagnosis of abnormal cardinal systemic venous return without other heart defects: a case series. *Prenat Diagn*. 2011;31:380-8.
15. Esmer AÇ, Yüksel A, Calı H, Özürmeli M, Omeroğlu RE, Kalelioğlu I, et al. Prenatal diagnosis of persistent left superior vena cava and its clinical significance. *Balkan Med J*. 2014;31:50-4.
16. Özürmeli M, Büyükkurt S, Sucu M, Arslan E, Akçabay Ç, Mısırhoğlu S, et al. Prenatal diagnosis of persistent left superior vena cava: a retrospective study of associated congenital anomalies. *Turk J Obstet Gynecol*. 2019;16:23-8.
17. Cao Q, Zhen L, Pan M, Han J, Yang X, Xu LL, et al. Prenatal persistent left superior vena cava in low population: not a benign vascular anomaly. *Taiwan J Obstet Gynecol*. 2022;61:459-63.
18. Kahramanoglu O, Demirci O, Uygunur I, Erol N, Schiattarella A, Rapisarda AMC. Persistent left superior vena cava with and without right superior vena cava: significance of prenatal diagnosis. *Pediatr Cardiol*. 2024;45:377-84.
19. Machevin-Surugue E, David N, Verspyck E, Labadie G, Blaysat G, Durand I, et al. Dilated coronary sinus in prenatal echocardiography; identification, associations and outcome. *Prenat Diagn*. 2002;22:898-902.
20. Choi EY, Hong SK, Jeong NY. Clinical characteristics of prenatally diagnosed persistent left superior vena cava in low-risk pregnancies. *Prenat Diagn*. 2016;36:444-8.
21. Minsart AF, Boucoiran I, Delrue MA, Audibert F, Abadir S, Lapierre C, et al. Left superior vena cava in the fetus: a rarely isolated anomaly. *Pediatr Cardiol*. 2020;41:230-6.
22. Li TG, Wu WR. Prenatal diagnosis of type I persistent left superior vena cava and its correlation with congenital cardiac comorbidities. *J Obstet Gynaecol*. 2025;45:2513618.
23. Wei R, Gong J, Ling W, Wu Q, Lyu G, Wang Y, et al. Prenatal ultrasound diagnosis and prognosis of persistent left superior vena cava: a 10-year retrospective cohort study at a single center in China. *Front Med (Lausanne)*. 2026;13:1743489.
24. Yang X, Su XH, Zeng Z, Fan Y, Wu Y, Guo LL, et al. Integrated analysis of comorbidity, pregnant outcomes, and amniotic fluid cytogenetics of fetuses with persistent left superior vena cava. *World J Cardiol*. 2023;15:500-7.
25. Cruz Lemini M, Juárez-Martínez I, Mendez A, Rebolledo C, Cruz-Martínez R. OP18.04: Outcomes and chromosomal abnormalities in fetuses prenatally diagnosed with isolated persistent left superior vena cava. *Ultrasound Obstet Gynecol*. 2015;46(Suppl 1):107.